SPL for PLR

SPL Workshop

April 27, 2006

Steps for Creating SPL

- Label
  - Create label with Highlights
  - Resources – Physician Labeling Rule and Guidance
- Table
  - Fill in the table for the Highlights Data Elements
  - Resources
    - Selecting Terms for Highlights Data Elements
    - Controlled Terminology (www.fda.gov/oc/datacouncil)
- Able
  - Then you are able create SPL
  - Resource – SPL Implementation Guide for Highlights

SPL Update for PLR

- Full prescribing information (FPI)
- FPI contents
- Highlights text
- Company and approval data elements
- Indication and usage data elements
- Interactions and adverse reaction data elements
- Pharmacological class data elements

Header References

- Reference to stylesheet
  - http://www.fda.gov/oc/datacouncil/stylesheets/spl/spl.xsl
- Reference to schema
  - http://www.fda.gov/oc/datacouncil/schemas/spl/spl.xsd

Full Prescribing Information

- Use appropriate LOINC codes for sections and subsections
- Order sections and subsections as described in the regulations
- Use the section and subsection title as described in the regulations including numbering
  - Section and subsection headings bold
- Tag recent major changes in the labeling text using styleCode text tag
  - <text>This is an example of text that is not changed.<content styleCode="xmChange">This is an example of text that is a recent major change</content>This is an example of changed text that is not considered a recent major change</text>

FPI Contents Stylesheet

FULL PRESCRIBING INFORMATION: CONTENTS[*]

[* Sections or subsections omitted from the full prescribing information are not listed”]

FPI Contents

- FPI Contents is created from FPI sections and subsections title
- FPI contents uses title from the FPI contents

Highlights Text Stylesheet

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use [Proprietary names] safely and effectively. See full prescribing information for [proprietary name].

[PROPRIETARY NAME] ([nonproprietary name])
Dosage form: [Dosage form display name]
Route of administration: [Route of administration display name]
[DEA schedule display name]
Initial U.S. Approval: [Approval year]

[Box Warning highlights text is placed here]
----------**RECENT MAJOR CHANGES**----------
[Recent major changes highlights text]
----------**INDICATIONS AND USAGE**----------
[Indications and usage highlights text]
----------**DOSAGE AND ADMINISTRATION**----------
[Dosage and Administration highlights text]
----------**DOSAGE FORMS AND STRENGTHS**----------
[Dosage forms and strengths highlights text]
----------**CONTRAINDICATIONS**----------
[contraindication highlights text]
----------**WARNINGS AND PRECAUTIONS**----------
[warnings and precautions highlights text]
----------**ADVERSE REACTIONS**----------
[adverse event highlight text]
To report SUSPECTED ADVERSE REACTIONS, contact ([represented organization name]) at ([assigned entity telecom] and [assigned entity telecom]) or [if human prescription drug, then FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*]
----------**DRUG INTERACTIONS**----------
[drug interaction highlights text]
----------**USE IN SPECIFIC POPULATIONS**----------
[Use in specific population highlights text]

[Patient counseling statement here]

Revised: [effectiveTime]

Highlights Text in SPL

- There are up to 10 sections for Highlights text:

  - Box Warning
  - Recent Major Changes
  - Indications and Usage
  - Dosage and Administration
  - Dosage forms and Strengths
  - Contraindications
  - Warnings and Precautions
  - Adverse Reactions
  - Drug Interactions
  - Use in Specific Populations

- The Highlights text is recorded in the appropriate main section (not subsection) of the SPL for example - The text for the Indications and Usage Highlights is placed in the Indications and Usage section of SPL. If there are more than one indication, the Highlights text is in the main section.

Highlights Text

<excerpt>
    <highlight>
        <text></text>
    </highlight>
</excerpt>

Highlights Data Elements

- Company and approval
  - Company name
  - Reporting information
  - Year of initial approval
- Indication and usage
  - Intent of Use
  - Indication category
  - Indication
  - Precondition category
  - Precondition
  - Adjunct treatment
  - Maximum dose
  - Limitation of use category
- Interaction and adverse reaction
  - Issue category
  - Contributing factor
  - Type of consequence
  - Consequence
- Pharmacological class

Highlights Data Elements Terminologies

- Intent of Use
- Indication category
- Precondition category
- Medical condition
- Sex
- Race
- Limitation of use/issue category
- Ingredient
- Product
- Contributing factor
- Type of consequence
- Pharmacokinetic effect
- Mechanism of action
- Physiologic effect
- Structural class

Company and Approval Information

- Data elements
  - Company name for display in Highlights
  - Contact information for reporting adverse reaction for display in Highlights
    - Phone number (displayed first)
    - Web address
  - Year of initial US approval for display in Highlights

Company and Approval Information

```
<legalAuthenticator>
      <time/>
      <assignedEntity>
            <telecom>phone number here</telecom>
            <telecom>web address here</telecom>
            <representedOrganization>
               <name>company name here</name>
            </representedOrganization>
      </assignedEntity>
</legalAuthenticator>
<verifier>
     <time value=“initial US approval year here"/>
     <assignedEntity/>
</verifier>
```

Indications and Usage Data Elements Stylesheet

Indication and Usage						
Indication			Usage			
Indication concept	**Intent of use**	**Maximum Dose**	**Use category**	**Precondition category**	**Precondition**	**Section**
			Condition of Use			
			Limitation of Use			

Indication Data Elements Location

- Indications and Usage section
  - Under the main section if only one indication
  - For multiple indications, data elements for each indication are in the subsection for the indication

Intent of Use

- Highlights - drug is indicated for the treatment, prevention, mitigation, cure or diagnosis of a recognized disease of condition
- Terminology – only three choices
  - Treatment (TREAT) – HL7
  - Prophylaxis (PRYLX) – HL7
  - Diagnostic (DIAG) – HL7

Indication Category

- Highlights – indication is a disease or condition
- Terminology – only one choice
  - Medical problem - LOINC

Indication

- Highlights - a recognized disease or condition or of a manifestation of a recognized disease or condition, or symptoms associated with a recognized disease or condition.
- Terminology
  - Medical condition - Problem List Subset

Indication Data Elements

```
<reason typeCode=“xxxx">
    <indicationObservationCriterion>
        <code code=“44100-6"
          codeSystem="2.16.840.1.113883.6.1"
          displayName=“Medical Problem"/>
        <value code=“xxxx"
          codeSystem="2.16.840.1.113883.6.96"
          displayName=“xxxx"/>
    </indicationObservationCriterion>
</reason>
```

[Intent of use]

[Indication category]

[Indication]

Maximum Dose

- Highlights - The upper limit of the dosage of a drug beyond which safety and effectiveness has not been established, or beyond which increasing the dose does not result in increasing effectiveness (amount per time)
- Terminology
  - Unit of amount – UCUM
  - Unit of time – UCUM

Maximum Dose

```
<highlight>
    <subject>
        <substanceAdministration>
            <maxDoseQuantity>
                <numerator value=“xxx" unit=“xxx"/>
                <denominator value=“xxx"
                  unit=“xxx"/>
            </maxDoseQuantity>
        </substanceAdministration>
    </subject>
</highlight>
```

Usage Stylesheet

Usage			
Use category	**Precondition category**	**Precondition**	**Section**

Condition of Use Location

- Condition of Use
  - Specific population
  - Adjunct treatment
  - Screening/monitoring test
- Condition of Use placed under the section or subsection where they are described

Condition of Use
Specific Population

- Highlights - use of the drug in a selected subgroup of the larger population related to a characteristic of the patient.
- Terminology
  - Precondition category – only 4 choices - LOINC
    - Medical condition, Sex, Race , Age
  - Precondition
    - Medical condition - Problem List Subset
    - Sex - NCI Thesaurus
    - Race - NCI Thesaurus
    - Age – range - high and low age, ≥ - low value only, ≤ - high value only

Specific Population

```
<precondition>
    <observationCriterion>
        <code code="xxx"
          codeSystem="2.16.840.1.113883.6.1"
          displayName="xxx"/>
        <value xsi:type="CE" code="xxx"
          codeSystem="2.16.840.1.113883.3.xxx"
          displayName="xxx"/>
    </observationCriterion>
</precondition>
```

[Precondition category]

[Precondition]

Condition of Use
Adjunct Treatment

- Highlights - use of the drug only in conjunction with another drug as an adjunct treatment.
- Terminology
  - "Precondition"
    - Ingredient – FDA SRS UNII
    - Product – FDA DRLS NDC
    - Class – VA NDF-RT

Adjunct Treatment

```
<precondition>
    <substanceAdministrationCriterion>
        <consumable>
            <administrableMaterial>
                <playingMaterialKind>
                    <code code="xxx"
                    codeSystem="2.16.840.1.113883.xxx"
                    displayName=“xxx"/>
                </playingMaterialKind>
            </administrableMaterial>
        </consumable>
    </substanceAdministrationCriterion>
</precondition>
```

[Adjunct treatment]

Condition of Use
Screening or Monitoring Test

- Highlights
  - the necessity of specific tests for the selection or monitoring of patients who need the drug.
- Terminology
  - Precondition
    - Screening or monitoring test - LOINC

Screening or Monitoring Test

```
<componentOf>
    <protocol>
        <component>
            <monitoringObservation>
                <code code=“xxx”
                codeSystem="2.16.840.1.113883.6.1"
                displayName=“xxxxx"/>
            </monitoringObservation>
        </component>
    </protocol>
</componentOf>
```

[Screening/monitoring test]

Limitation of Use Location

- Limitation of Use placed under the section or subsection where they are described

Limitation of Use

- Highlights - information regarding uncertainty about anticipated clinical benefits or that the therapeutic benefits of the product do not generally outweigh the risks.
- Terminology
  - Limitation of Use category - NCI Thesaurus
  - Precondition category – only 4 choices - LOINC
    - Medical condition, Sex, Race, Age
  - Precondition
    - Medical condition - Problem List Subset
    - Sex - NCI Thesaurus
    - Race - NCI Thesaurus
    - Age – range - high and low age, ≥ - low value only, ≤ - high value only

Limitation of Use

```
<subjectOf>
    <issue>                                                    [Limitation of use category]
        <code code="xxx"
          codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="xxxx"/>
        <subject>
            <observationCriterion>
                <code code="xxx"                               [Precondition category]
                  codeSystem="2.16.840.1.113883.6.1"
                  displayName="xxxx"/>
                <value xsi:type="CE" code="xxx"
                  codeSystem="2.16.840.1.113883.3.xx.x"
                  displayName="xxx"/>
                                                               [Precondition]
            </observationCriterion>
        </subject>
    </issue>
</subjectOf>
```

Interactions and Adverse Reactions Stylesheet

Interaction and Adverse Reactions			
Contributing Factor	**Type of Consequence**	**Consequence**	**Labeling Section**
Interactions			
	Type of Consequence	**Consequence**	**Labeling Section**
Adverse reactions			

Interactions and Adverse Reactions Location

- Each interaction and adverse reaction coded in a subsection under a labeling section
  - Box Warning
  - Indications and Usage
  - Contraindications
  - Warnings and Precautions
  - Adverse Reactions
  - Drug Interactions
  - Use in Specific populations

Interactions and Adverse Reactions

- Highlights - interactions that have a contributing factor such as food or another drug and a consequence such as a medical condition or an adverse reaction.
- Issue code – only two choices - NCI Thesaurus
  - Interaction
  - Adverse reaction
- Contributing factor*
  - Food or drug ingredients - FDA SRS UNII
  - Drug product - FDA DRLS NDC
  - Drug class - VA NDF-RT
  - General - NCI Thesaurus
- Type of consequence – only two choices - NCI Thesaurus
  - Pharmacokinetic effect*
  - Patient problem
- Consequence
  - Pharmacokinetic effects* - NCI Thesaurus
  - Medical condition – Problem List Subset

*Only for interactions

Issue Code

```
<subjectOf>
    <issue>                                                    [Issue code]
        <code code="xxx"
          codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="xxxx"/>
        <subject>
            ….
        </subject>
    </issue>
</subjectOf>
```

Contributing Factor

```
<issue>
  <subject>
    <substanceAdministrationCriterion>
      <consumable>
        <administrableMaterial>
          <playingMaterialKind>
            <code code="xxx"
          codeSystem="xxx“
          displayName=“xxxx"/>
          </playingMaterialKind>
        </administrableMaterial>
      </consumable>
    </substanceAdministrationCriterion>
  </subject>
</issue>
```

[Contributing factor]

Consequence

```
<risk>
    <consequenceObservation>
        <code code= “xxxx"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName=“xxxx"/>
        <value xsi:type="CE"
        code= “xxxx"
        codeSystem="xxx"
        displayName=“xxxx"/>
    </consequenceObservation>
</risk>
```

[Type of consequence]

[Consequence]

Pharmacological Class Stylesheet

Established Pharmacological Class	
Substance	**Pharmacological Class**

Pharmacological Class Location

- Data elements under a specific ingredient or product data element
  - Each ingredient or product can belong to zero to many classes

Pharmacological Class

- Highlights - Active ingredients and products may be described by pharmacological class.
- Terminology
  - Mechanism of action - VA NDF-RT
  - Physiologic effect - VA NDF-RT
  - Structural class - VA NDF-RT

Pharmacological Class by Ingredient

```
<activeIngredient>
  <activeIngredientSubstance>
    <asSpecializedKind>
      <generalizedPharmaceuticalClass>
          <code code="xxxx"
          codeSystem="2.16.840.1.113883.3.26.1.5"
          displayName="xxx"/>
      </generalizedPharmaceuticalClass>
    </asSpecializedKind>
  </activeIngredientSubstance>
</activeIngredient>
```

Pharmacological Class by Product

```
<manufacturedMedicine>
    <asSpecializedKind>
        <generalizedPharmaceuticalClass>
            <code code="xxx"
            codeSystem="2.16.840.1.113883.3.26.1.5"
            displayName="xxx"/>
        </generalizedPharmaceuticalClass>
    </asSpecializedKind>
</manufacturedMedicine>
```